REMARKS

Claims 1-21 are pending. Claims 2, 4, 6-15, and 17-21 have been withdrawn from consideration. Claims 1, 3, 5, and 16 have been examined. Claim 16 was objected to for being dependent from a non-elected claim. Claims 1, 3, 5, and 16 were provisionally rejected under 35 U.S.C. § 101. Claims 1, 3, 5, and 16 were rejected under 35 U.S.C. § 102.

Amendments to the Specification

Applicants have amended the specification to refer to each drawing. In addition, Applicants have amended the brief description of Figure 4 to clearly describe the subject matter of this figure. No new matter has been added by these amendments.

Claim Objections

Claim 16 was objected to for depending from a non-elected claim. Claim 16 has been canceled and this rejection therefore is moot.

Rejection under 35 U.S.C. § 101

Claims 1, 3, 5, and 16 were provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as that of claims 1, 3, 5, and 16 of co-pending U.S. Patent Application No. 09/559,622 ("the '622 application"). As claim 16 has been canceled, the rejection of this claim is moot. Applicants note that the remaining claims, claims 1, 3, and 5, are directed to a non-elected invention in the '622 application and Applicants agree

to cancel these claims in reply to the next Office Action issued in connection with that application.

Rejection under 35 U.S.C. § 102(b)

Claims 1, 3, 5, and 16 were rejected under 35 U.S.C. § 102(b) as being anticipated by Blakely et al. (*Nature* 354:66-70, 1991; "Blakely"), Corey et al. (*Proc. Natl. Acad. Sci. USA* 91:1188-1192, 1994; "Corey"), Demchyshyn et al. (*Proc. Natl. Acad. Sci. USA* 91:5158-5162, 1994; "Demchyshyn"), Olde et al. (*J. of Molecular Neuroscience* 8:53-62, 1997; "Olde"), and Ramamoorthy et al. (*Proc. Natl. Acad. Sci. USA* 90:2542-2546, 1993; "Ramamoorthy"). The Office states that the references "each teach the cloning and characterization of [a] serotonin anion channel." As is noted above, Applicants have canceled claim 16 and the rejection of this claim is moot. Applicants traverse the 35 U.S.C. § 102(b) rejection of claims 1, 3, and 5 as follows.

To anticipate a claim, the prior art has to teach each and every element set forth in that claim. None of the cited references teaches a substantially pure nucleic acid sequence encoding a serotonin-gated anion channel as required by claim 1. Blakely teaches the cloning and expression of a functional serotonin transporter from rat brain; Corey and Demchyshyn teach a Drosophila serotonin transporter; Ramamoorty teaches a human serotonin transporter; and Olde teaches a G-protein-coupled serotonin receptor. Serotonin transporters and G-protein-coupled serotonin receptors are not serotonin-gated anion channels. The specification, at page 16, lines 5-7, defines a serotonin-gated anion

channel as:

> [A] channel whose opening is regulated by serotonin binding to the channel. The opening of the channel selectively permits passage of anions from one side of the channel to the other. (Emphasis added)

In contrast, the serotonin transporters described by Blakely, Corey, Demchyshyn, and Ramamoorthy transport serotonin across a membrane and, therefore, are clearly distinct from the presently claimed serotonin-gated anion channels. Likewise, the receptors of Olde are also distinct from the claimed invention. As is stated by Olde at page 53, in the first paragraph, these receptors, upon binding serotonin, "exert their action through interaction with G-proteins." None of the cited references teach the presently claimed invention, namely, a substantially pure nucleic acid sequence encoding a serotonin-gated anion channel. The 35 U.S.C. § 102 rejection of claims 1, 3, and 5 may be withdrawn.

CONCLUSION

Applicants submit that the application is in condition for allowance and such action is respectfully requested.

Applicants note that the Office Action was mailed to the incorrect address. Effective immediately, please address all communication in this application to:

Kristina Bieker-Brady, Ph.D.
Clark & Elbing LLP
101 Federal Street
Boston, MA 02110

Enclosed are clean and "marked-up" versions of the replacement paragraphs.

Also enclosed is a petition to extend the period for replying for two months, to an including March 22, 2003.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: March 14, 2003

Kristina Bieker-Brady, Ph.D.
Reg. No. 39,109

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
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01997.521003 Reply to Office Action dated 10.22.02.doc

U.S. Serial No. 09/717,743
Version of Replacement Paragraphs Showing Changes Made

Amend the paragraph beginning on page 20, line 21 as follows.

Fig. 4 shows the structure of the *C. elegans* MOD-1 [cDNA] amino acid sequence.

Amend the paragraph beginning at page 23, line 15 as follows.

The *mod-1* mutants, as described in the previous section, were further characterized using this technique. Animals carrying the n3034 mutation (Fig. 7 and Fig. 8) exhibited a dominant phenotype of insensitivity to exogenous serotonin in liquid locomotion assays. Animals carrying the ok103 mutation (Fig. 5 and Fig. 6) exhibited a recessive phenotype of insensitivity to exogenous serotonin in liquid locomotion assays.

Amend the paragraph beginning at page 23, line 23 as follows.

Both the wild type (Fig. 2), and mutant *mod-1* cDNA have been obtained. The dominant serotonin resistance phenotype of animals carrying the *mod-1(n3034)* allele was used to genetically map *mod-1(n3034)* to a 0.7 map-unit interval on chromosome V. Deficiency analysis showed that the dominant serotonin resistance phenotype is not due to a haploinsufficiency of the *mod-1* locus. The recessive nature of the serotonin resistance phenotype at early time points was exploited to perform standard transformation rescue experiments, and subsequently, the gene was cloned (Fig. 1).

Amend the paragraph beginning at page 24, line 9 as follows.

The protein encoded by the *mod-1* open reading frame responsible for the rescue is structurally similar to ligand-gated ion channels that belong to the nicotinic acetylcholine receptor (nAchR) family (Fig. 3 and Fig. 4). The nAchR family members are all pentameric channels with large N-terminal extracellular ligand-binding domains, four highly conserved transmembrane domains (M1-M4), and relatively divergent cytoplasmic domains between M3 and M4. nAchR family members include channels gated by acetylcholine, glycine, GABA, avermectin, and serotonin. Within the members of the nAchR family, structure-function analysis has been performed primarily on the acetylcholine receptor, but many structural and functional parallels have been seen with the other family members as well. In addition, chimeric channel studies show that there is a great deal of conservation at the functional level, even across the different ligand-gated members of the family. The M2 domains of the various subunits are predicted to line the pore of the channels. Site-directed mutagenesis studies of residues within this domain have demonstrated that ion specificity and modulation of the magnitude and frequency of current flux are determined, at least in part, by the residues that line the pore and those that are immediately adjacent to the pore on both the extracellular and cytoplasmic sides. Based on primary sequence analysis, MOD-1 appears to be equally divergent from all cloned nAchR family members.

Amend the paragraph beginning at page 25, line 5 as follows.

MOD-1 was heterologously expressed in *Xenopus* oocytes, injected with 50 nl of *C. elegans* RNA, or MOD-1 was expressed in HEK cells transiently transfected by calcium phosphate precipitation. Forty-eight to 72 hours later, the cells or oocytes were screened under a voltage clamp (Figs. 9A-9C). Application of 100 nM serotonin elicited large inward currents at a holding potential of -70 mV. Uninjected oocytes and nontransfected cells had no response to 10 μM serotonin. Application of 1 mM of other agonists of ligand-gated ion channels, such as acetylcholine, GABA, or glycine elicited little or no response from the MOD-1 channel.

Amend the paragraph beginning at page 26, line 2 as follows.

Ion selectivity was determined by measuring changes in the reversal potential (voltage at which the serotonin response changes from an inward, negative, to an outward, positive, current) in response to varying the ionic composition of the bath solution. The reversal potential was insensitive to changes in cations (Na^+ or K^+), but shifted by approximately 50 mV for each 10-fold change in extracellular chloride concentration (Fig. 10).

Clean Version of Replacement Paragraphs After Entry of Amendment

Amend the paragraph beginning on page 20, line 21 as follows.

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